ATTACHMENT
E

C T F A

THE COSMETIC, TOILETRY, AND FRAGRANCE ASSOCIATION

October 15, 1999

Charles J. Ganley, MD
Director
Division of OTC Drug Products (HFD-560)
Office of Drug Evaluation V
Center for Drug Evaluation and Research
9201 Corporate Boulevard - Room S212
Rockville, MD 20850

E. EDWARD KAVANAUGH
PRESIDENT

Re: Docket No. 78N-0038

Dear Dr. Ganley:

We want to thank you for the opportunity to meet with you and other Food and Drug Administration officials at the Sunscreen Working Group Meeting scheduled for October 26, 1999 to discuss the testing and labeling of high-SPF products. As you know we strongly believe these products provide a necessary and important public health benefit to consumers.

We are pleased that you are planning presentations by FDA staff on the seven points raised in your letter of September 2, 1999 regarding SPF testing, and look forward to a discussion of these issues with the Agency. We would appreciate a minor modification in the draft agenda to give an industry representative five minutes to describe a typical SPF test before beginning the FDA presentations. I think this would assist the discussion to follow.

Our objective for this meeting is to respond to the issues the agency has raised about the determination of high sun protection factor (SPF) values outlined in your letter of September 2, 1999 and how this information may be communicated to consumers.

As the enclosed documentation indicates, the comments submitted by CTFA on March 21, 1994 in response to the tentative final monograph continue to represent our position regarding specifications for solar simulator spectral power distribution (see Exhibit D, CTFA comments of March 21, 1994), as well as concurrence with a total irradiance limit of 1500 watts/meter^2. We intend to discuss in further detail the high-SPF standard sunscreen and the collaborative SPF testing data submitted in our 1994 comments and in a subsequent submission to the docket dated May 12, 1994, a copy of which is also enclosed.

In addition, we are submitting additional data presented at the feedback meeting of July 22, 1999 to demonstrate that current SPF test methodologies can produce accurate and reproducible results for high SPF formulations, and to provide data to answer the agency's concerns regarding the number of test subject needed, the variability of the data, and the appropriate exposure increments for testing high SPF formulations.

1101 17TH ST., N.W., SUITE 300 WASHINGTON, D.C. 20036-4702
202.331.1770 FAX 202.331.1969
http://www.ctfa.org

The primary industry representatives who will participate in the presentations and discussions at this meeting are:

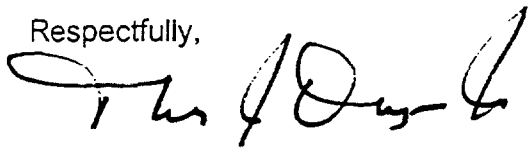
Patricia Agin, Ph.D., Research Director - Photobiology, Schering-Plough HealthCare Products
Thomas J. Donegan, Jr., Vice President - Legal & General Counsel, CTFA
Kenneth D. Marenus, Ph.D., Vice President, Biological Research, The Estee Lauder Companies

Industry concurs with the views of the January 4, 1999 letter from Schering-Plough Healthcare Products to FDA which amend its prior comments on an SPF Cap, a copy of which is enclosed. We believe there are populations who need products which provide very high sun protection and who count on the ability to distinguish such products as well. Furthermore, we believe existing test methodology exists to accurately and reproducibly distinguish them.

In preparation of the meeting, we are also enclosing a list of expected attendees. If you would like, we would be happy to provide you an updated list closer to the meeting date.

We thank the agency for this opportunity to work together. Please feel free to contact us if you have any questions in the meantime.

Respectfully,



Thomas J. Donegan, Jr.
Vice President - Legal & General Counsel

Enclosures:

1. Exhibit D from Comments of the Cosmetic, Toiletry, and Fragrance Association in Response to the Food and Drug Administration's tentative final monograph on OTC Sunscreen Drug Products, filed March 21, 1994,
2. Letter from CTFA to Dockets Management Branch, Food and Drug Administration, dated May 12, 1994,
3. Letter from Schering-Plough HeatlhCare Products to Dockets Management Branch, Food and Drug Administration, dated January 4, 1999,
4. "Testing High SPF Formulations - A Comparison of the Accuracy and Reproducibility of the Results of Testing Three High SPF Formulations by Two Methods: 1978 Proposed Monograph Method and 1993 Tentative Final Monograph Method", Schering-Plough Healthcare Products, September 1999, Appendix 1, and Appendix 2.
5. List of Meeting Attendees, expected to attend

TESTING HIGH SPF FORMULATIONS

A COMPARISON OF THE ACCURACY AND REPRODUCIBILITY OF THE RESULTS OF TESTING THREE HIGH SPF FORMULATIONS BY TWO METHODS: 1978 PROPOSED MONOGRAPH METHOD AND 1993 TENTATIVE FINAL MONOGRAPH METHOD

SCHERING-PLOUGH HEALTHCARE PRODUCTS

SEPTEMBER 1999

Introduction

The ability of current SPF test methods to produce accurate and reproducible SPF values for sunscreen products with SPFs >30 has been questioned by the Agency in its 1999 Final Rule. The data which were presented at the feedback meeting of July 22, 1999 are provided in more detail in Tables 1-3 and are discussed below. The protocols used for testing these formulations are provided in Appendices 1 and 2, attached. The goals of this report are 1) to demonstrate that the current existing SPF test methodologies can produce accurate and reproducible results for high SPF formulations and 2) to provide data which address the Agency's questions concerning information on the number of test subjects needed, the variability of the data, and the appropriate exposure increments for testing high SPF formulations.

Materials and Methods

Three high SPF formulations were tested according to the 1993 tentative final monograph very water-resistant test method (protocol, Appendix 1) and/or the 1978 proposed monograph waterproof test method (protocol, Appendix 2). Each panel of data shown represents an autonomous test panel.

Formula 1: SPF >30 lotion

active ingredients:	homosalate
	octyl salicylate
	octyl methoxycinnamate
	oxybenzone
	avobenzone

Formula 2: SPF >40 lotion

active ingredients:	homosalate
	octyl salicylate
	octyl methoxycinnamate
	oxybenzone

Formula 3: SPF >40 lotion

active ingredients:	octocrylene
	octyl salicylate
	octyl methoxycinnamate
	oxybenzone

Results

The test data and data summaries are shown in Tables 1, 2 and 3. Table 1 compares the data obtained by testing the SPF >30 lotion by either the 1993 tentative final method or

by the 1978 proposed method. Table 2 includes data from two separate tests of an SPF >40 lotion by the 1978 proposed method in comparison to a panel of data on the same formulation obtained using the 1993 tentative final method. Table 3 includes data from two separate tests of an SPF >40 lotion, both tests conducted using the 1993 tentative final method. While the SPF 4 standard was tested as per the protocols, these data were all within expected limits and are not shown.

Discussion

The data shown in Table 1 include SPF test results for a formulation with an SPF >30, tested by the 1978 proposed monograph test method as well as by the method described in the 1993 tentative final monograph (TFM). These data illustrate that both methods were able to determine that the formulation had an SPF of above 30, using either the statistical analysis method in the 1978 monograph ("Mean SPF") or the statistical method described in the tentative final monograph ("FM SPF"). The data indicate that the formulation could be labeled as an SPF >30 in both cases.

The data in Table 1 also serve to illustrate that the use of either the series of 5 exposures at 25% increments (1978 proposed method) or the TFM 15% increments (series of 7 exposures) results in similar SPF values. Either data set would qualify the formulation for labeling as an SPF 30 product.

The data shown in Table 2 include three panels of SPF test results for a formulation with an SPF >40, tested twice by the 1978 proposed monograph test method as well as once by the method described in the 1993 tentative final monograph. These data illustrate that both the proposed and the tentative final methods were able to demonstrate that the formulation had an SPF of above 40, using either the statistical analysis method in the 1978 monograph (Mean SPF) or the statistical method described in the tentative final monograph (FM SPF). The mean values for the three data sets are remarkably similar. Calculating the final SPF (FM SPF) according to the tentative final monograph for each panel indicates that the formulations could be labeled as an SPF >40 regardless of the test method used.

The data in Table 2 also illustrate that the use of the 25% exposure increments or the 15% increment series resulted in similar SPF values for the panel. Note also that these data sets show that the variability of the data fits within the acceptable statistical parameters outlined in either the proposed or the tentative final monograph's statistical requirements, regardless of the exposure increment series used. For that reason, we feel that the current methodology is adequate relative to the exposure series proposed. However, we do not feel that the series of seven exposures (with half-increments around the mid point) provides more precise data, due to the inherent biological variability of subjects' skin responses. The 25% increment series appears to be as accurate for a full panel of subjects as is the smaller increment series. Both methods can provide acceptable data.

The data shown in Table 3 include SPF test results for a second formulation with an SPF >40, tested in two separate panels by the method described in the 1993 tentative final monograph. These data illustrate that for both panels, the method was able to demonstrate that the formulation had an SPF of above 40, using either the statistical analysis method in the 1978 monograph (Mean SPF) or the statistical method described in the tentative final monograph (FM SPF). Note that the mean value for the two panels is almost identical, and that the final SPF calculated according to the TFM for either panel indicates that the formula qualifies for labeling as an SPF 45.

These data also show that the variability of the data is not outside what is expected in this type of test and that the data fit within the desired statistical parameters for a well formulated sunscreen product with an SPF >40.

The data sets (Tables 1, 2 and 3) also can be used to address the Agency's question concerning the number of test subjects needed in a panel. As one can see from the Tables, the number of subjects (20-25) seems sufficient for the purpose of obtaining valid data for high SPF products, as the statistical variability is acceptable according to the analyses methods described in the sunscreen monographs.

Conclusions

The data illustrate that either the 1978 proposed test method or the 1993 tentative final method can provide accurate and reproducible results for high SPF formulations. Further, these results can be achieved with panels of 20-25 subjects without an unacceptable level of variability.

The data contained in Tables 1, 2 and 3 also serve to illustrate that formulations tested under the 1978 proposed monograph and labeled with SPF values according to that test method were determined to provide a level of protection not significantly different than the SPF level obtained using the tentative final method. Marketed products tested by the 1978 proposed method, therefore, would not pose a public health threat or a safety hazard based on the data shown; the necessity to retest these products is called into question-- as long as full panels of data meeting the appropriate statistical parameters exist to support their efficacy and labeling.

Based on the results shown in this study, the current methods for testing sunscreen formulations have been shown to be appropriate for testing formulations with SPFs above 30. Either the 1978 proposed method (series of 5 exposures at 25% increments) or the 1993 TFM method (series of 7 exposures, including 2 half-increment exposures, at 15% increments) can provide satisfactory data to determine a valid product SPF.

References

Australia/New Zealand Standard: Sunscreen Products-Evaluation and Classification, AS/NZS 2604:1997.
COLIPA: Sun Protection Factor Test Method, ref. 94/289, October 1994.
Federal Register: May 21, 1999 (Volume 64, Number 98), Final Rule, pp. 27666-27693.
Federal Register: May 12, 1993 (Volume 58, Number 90), Tentative Final Monograph pp. 28194-28302.
Federal Register: August 25, 1978 (Volume 43, Number 166), Proposed Rulemaking pp. 38206-38269.
Japan Cosmetic Industry Association Standard SPF Test Method, Revised, May 18, 1999.

TABLE 1
SPF TEST SUMMARY REPORT

FORMULA: SPF > 30 Lotion
Active Ingredients: OXYBENZONE, HOMOSALATE, OCTYL SALICYLATE, OCTYL METHOXYCINNAMATE, AVOBENZONE

Protocol: 1993 Tentative Final Monograph Method
Description: VERY WATER RESISTANT SPF

Subject	MED	Ctl MED		Actual SPF
1	609	16		38.06
2	312	16		19.50
3	488	16		30.50
4	240	10		24.00
5	300	8		37.50
6	750	25		30.00
7	469	13		36.08
8	488	16		30.50
9	750	20		37.50
10	600	25		24.00
11	938	20		46.90
12	938	25		37.52
13	<480	25		<19.20
14	750	20		37.50
15	>938	20		>46.90
16	1172	25		46.88
17	1453	39		37.26
18	1463	31		47.19
19	750	20		37.50
20	1163	31		37.52
21	744	20		37.20
22	938	25		37.52

TEST SUMMARY

Mean SPF: 35.53 **FM SPF: 32**
Number Tested: 22 Number Calculated: 20
Standard Deviation: 6.55
Percent Standard Error of Mean: 5.3

Protocol: 1978 Proposed Monograph Method
Description: WATERPROOF SPF

Subject	MED	Ctl MED		Actual SPF
1	720	16		45.00
2	<461	13		<35.46
3	900	20		45.00
4	576	16		36.00
5	<608	16		<38.00
6	560	16		35.00
7	920	20		46.00
8	800	20		40.00
9	744	16		46.50
10	1006	31		32.45
11	560	16		35.00
12	805	20		40.25
13	599	13		46.08
14	700	20		35.00
15	651	16		40.69
16	644	16		40.25
17	455	13		35.00
18	700	20		35.00
19	700	20		35.00
20	805	25		32.20
21	599	16		37.44
22	609	25		24.36
23	599	20		29.95

TEST SUMMARY

Mean SPF: 37.72 **FM SPF: 35**
Number Tested: 23 Number Calculated: 21
Standard Deviation: 5.89
Percent Standard Error of Mean: 3.4

TABLE 2
SPF TEST SUMMARY REPORT

FORMULA: SPF >40 Lotion
Active Ingredients: OXYBENZONE, HOMOSALATE, OCTYL-METHOXYCINNAMATE, OCTYL SALICYLATE

Protocol: 1978 Proposed Monograph Method
Description: WATERPROOF SPF (Panel 1)

Subject	MED	Ctl MED		Actual SPF
1	624	13		48.00
2	960	20		48.00
3	960	20		48.00
4	960	16		60.00
5	768	16		48.00
6	499	13		38.38
7	<614	20		<30.70
8	960	20		48.00
9	<492	25		<19.68
10	960	20		48.00
11	768	20		38.40
12	768	20		38.40
13	768	16		48.00
14	<768	25		<30.72
15	960	20		48.00
16	<768	25		<30.72
17	1200	20		60.00
18	960	20		48.00
19	1200	20		60.00
20	1500	25		60.00
21	960	16		60.00
22	768	20		38.40
23	1200	25		48.00
24	768	20		38.40
25	<319	13		<24.54

TEST SUMMARY
Mean SPF: 48.60 **FM SPF: 45**
Number Tested: 25 Number Calculated: 20
Standard Deviation: 7.86
Percent Standard Error of Mean: 3.7

Protocol: 1978 Proposed Monograph Method
Description: WATERPROOF SPF (Panel 2)

Subject	MED	Ctl MED		Actual SPF
1	1406	20		70.30
2	1125	25		45.00
3	900	16		56.25
4	900	20		45.00
5	576	16		36.00
6	900	20		45.00
7	900	20		45.00
8	720	20		36.00
9	720	16		45.00
10	900	25		36.00
11	1125	25		45.00
12	720	16		45.00
13	1125	20		56.25
14	1758	25		70.32
15	1125	25		45.00
16	1125	25		45.00
17	1406	25		56.24
18	720	20		36.00
19	1125	25		45.00
20	1125	25		45.00

TEST SUMMARY
Mean SPF: 47.42 **FM SPF: 44**
Number Tested: 20 Number Calculated: 20
Standard Deviation: 9.91
Percent Standard Error of Mean: 4.8

Protocol: 1993 Tentative Final Monograph Method
Description: VERY WATER RESISTANT SPF

Subject	MED	Ctl MED		Actual SPF
1	1744	31		56.26
2	1125	25		45.00
3	783	16		48.94
4	1488	25		59.52
5	828	16		51.75
6	783	20		39.15
7	<461	16		<28.81
8	1488	25		59.52
9	1125	20		56.25
10	1125	25		45.00
11	576	16		36.00
12	<681	20		<34.05
13	1035	20		51.75
14	978	20		48.90
15	<851	20		<42.55
16	<851	25		<34.04
17	1604	39		41.13
18	<851	31		<27.45
19	783	20		39.15
20	1488	25		59.52
21	900	20		45.00
22	1369	25		54.76
23	1190	20		59.50
24	900	16		56.25
25	720	16		45.00

TEST SUMMARY
Mean SPF: 49.92 **FM SPF: 46**
Number Tested: 25 Number Calculated: 20
Standard Deviation: 7.68
Percent Standard Error of Mean: 3.4

TABLE 3
SPF TEST SUMMARY REPORT

FORMULA: SPF >40 Lotion
Active Ingredients: OXYBENZONE, OCTYL SALICYLATE, OCTOCRYLENE, OCTYL METHOXYCINNAMATE

Protocol: Tentative Final Monograph Method (Panel 1)
Description: VERY WATER RESISTANT SPF

Subject	MED	Ctl MED		Actual SPF
1	1000	20		50.00
2	<605	20		<30.25
3	<605	31		<19.52
4	1058	16		66.13
5	783	16		48.94
6	595	13		45.77
7	<855	20		<42.75
8	978	20		48.90
9	770	16		48.13
10	1485	25		59.40
11	736	20		36.80
12	685	16		42.81
13	685	16		42.81
14	1327	25		53.08
15	1056	25		42.24
16	685	16		42.81
27	1320	39		33.85
18	800	16		50.00
19	1056	20		52.80
20	845	20		42.25
21	1056	25		42.24
22	845	16		52.81
23	598	10		59.80

TEST SUMMARY

Mean SPF: 48.08
Number Tested: 23
Standard Deviation: 7.91
Percent Standard Error of Mean: 3.8

FM SPF: 45
Number Calculated: 20

Protocol: Tentative Final Monograph Method (Panel 2)
Description: VERY WATER RESISTANT SPF

Subject	MED	Ctl MED		Actual SPF
1	800	20		40.00
2	1000	25		40.00
3	598	13		46.00
4	1000	20		50.00
5	870	20		43.50
6	1323	25		52.92
7	952	16		59.50
8	1035	20		51.75
9	1294	20		64.70
10	1035	20		51.75
11	>950	16		>59.38
12	626	16		39.13
13	1204	25		48.16
14	828	20		41.40
15	626	13		48.15
16	950	20		47.50
17	1035	20		51.75
18	963	20		48.15
19	673	13		51.77
20	900	20		45.00
21	1604	31		51.74

TEST SUMMARY

Mean SPF: 48.64
Number Tested: 21
Standard Deviation: 6.43
Percent Standard Error of Mean: 3.0

FM SPF: 46
Number Calculated: 20